```
     10        20        30        40        50        60        70
GGAGGTATAGGAGCTCTCTTCGATTTAGCAAACCAGGAGTCCGAAGATCTAAGGAGAGCTGGGGTTTGACTCC
           SacI                                    BglII
     85        95        105       115       125       135       145
GAGAGCTCGAGCAGTCCCCAAGACCTGGTCTTGACTCACGAGTTAGACTCCACTCAGAGGCTGACTGTCTCCAGG
  SacI            PflMI
     XhoI             Tth111I
     160       170       180       190       200       210       220
GTCTACACCTCTAAGGGCGACACTGGCTCAAGCAGACTGCCGTTTTCTATATGGGATGAGCCTTCACAGGGCAG
     235       245       255       265       275       285       295
CCAGTTGGGATGGGTTGAGGTTTGGCTGTAGACATCAGAAACCCAAGTCAAATGCGCTTCAACCAGTAGAAAATT
     310       320       330       340       350       360       370
CACCAGCCCGCAGAGCTAAGGTTGGGTGGACATTAGGGTTGGTTGATCCAGGAGCTCAACAGTGTCCTCTGAGCC
                                                 SacI
     385       395       405       415       425       435       445
CCAGCTCCTTCTGCCCCACCCCACCATCTTCAGTGCTGCTTCCTCTCAAGGCCACAGCTGTAGTTGGCCAGGGGG
                                                    PvuII     BalI
                                                                BglI
     460       470       480       490       500       510       520
GCTTCATTATTTTTTGCTCCTGGGCAGTAGGAGGAAGAGAATGAATGTCTCTCCATGGGTCTTTCTTAGGAATGT
                                                   NcoI
     535       545       555       565       575       585       595
GGGAACTTTTTCCAGAAGTCTCTATGTCTTTTAGTTTGTGTTGGGTCACTTGCCCTTCCTGAACCACTTCCTGAC
     610       620       630       640       650       660       670
TCCTGGACAGGATGTGCACTGATGAGCTTAGCTTTGGGGATCTAATAGTGACTTTACAAAGCCTCTTTGAGAAGG
         ApaLI        EspI
     685       695       705       715       725       735       745
TGACATTGGAACCAAGGCTTGAGCAGACACAACAAAGATTGCAGGGAGGGGCATTGCAGGTGGAGGAAACGGCAC
                                                      BspMI-
     760       770       780       790       800       810       820
ATGCAAGAGCCCTGCGTGGGAGTGAGCTTGGTGTTTGGTCAATCAGTTGTCAGAGCACACCGGGCCCTGTCAGCA
                                                          ApaI
                                                          EcoO
```

Fig. 1A-1

```
      835       845       855       865       875       885       895
GGCACAGCCTGGGCCTGCTCTGAGTATGACAGAGAGCCCCTGGGAAGTTGTAGGTGGAGGAAAGACAGGTCATGA
        910       920       930       940       950       960       970
CTAGGAAAAAAGCAATCCCTCTGTTGTGGGGTGGAAGGAAGGTTGCAGTGTGTGTGAGAGAGAGACAAGACAGAC
      985       995      1005      1015      1025      1035      1045
AGACAGACACTTCTCAATGTTTACAAGTGCTCAGGCCCTGACCCGAATGCTTCCAAATTTACGTAGTTCTGGAAA
                              EcoO      BsmI+          SnaBI
     1060      1070      1080      1090      1100      1110      1120
ACCCCCTGTATCATTTTCACTACTCAAAGAAACCTCGGGAGTGTTTTCTTCTGAAAGGTCATCAGGTTTTGACTC
     1135      1145      1155      1165      1175      1185      1195
TCTGCTGTCTCATTTCTTCTTGCTGGTGGTGGTGATGGTTGCTTGTCCAGGCCCTGTCCCGCATCCTCTTGCCC
                                                  EcoO
     1210      1220      1230      1240      1250      1260      1270
CTGCAGAGGGATGAGTGTGTTGGGGCCTCACGAGTTGAGGTTGTTCATAAGCAGATCTCTTTGAGCAGGGCGCCT
PstI                EcoO                             BglII              NarI Ps
     1285      1295      1305      1315      1325      1335      1345
GCAGTGGCCTTGTGTGAGGCTGGAGGGGTTTCGATTCCCTTATGGAATCCAGGCAGATGTAGCATTTAAACAACA
tI                                                                 DraI
     1360      1370      1380      1390      1400      1410      1420
CACGTGTATAAAAGAAACCAGTGTCCGCAGAAGGTTCCAGAAAGTATTATGGGATAAGACTACATGAGAGAGGAA
     1435      1445      1455      1465      1475      1485      1495
TGGGGCATTGGCACCTCCCTTAGTAGGGCCTTTGCTGGGGGTAGAAATGAGTTTTAAGGCAGGTTAGACCCTCGA
                    EcoO                                  BspMI-
     1510      1520      1530      1540      1550      1560      1570
ACTGGCTTTTGAATCGGGAAATTTACCCCCAGCCGTTCTGTGCTTCATTGCTGTTCACATCACTGCCTAAGATG
     1585      1595      1605      1615      1625      1635      1645
GAGGAACTTTGATGTGTGTGTGTTTCTTTCTCCTCACTGGGCTCTGCTTCTTCACTTCCTTGTCAATGCAGAGAA
     1660      1670      1680      1690      1700      1710      1720
CAGCAGCAGGCACCAGAGGCAGGCCTTGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGG
                    StuI                                                BspMI
     1735      1745      1755      1765      1775      1785      1795
TAAGGGGCTGGCTGGGTCTGTCTTGGGTGTGGCCCTCTGGCGTGGCTCCCACAGGCAGCGGGTGCTGTGCTCA
                              ApaI
                              EcoO
```

Fig. 1A-2

Fig. 1A-3

```
           1810      1820      1830      1840      1850      1860      1870
GTCTTGTTTCTCATCTCTGCCAGTTAAGACTCCAGTATCAAGTGGCCTCGCTAGGGAAGGGTACTTGGCTAAGGA
           1885      1895      1905      1915      1925      1935      1945
TACAGGG.......(APPROX. 1000 BASES).............GGGAGCCAGCATGGGTGATGCCATTATGA
           1960      1970      1980      1990      2000      2010      2020
GTTATTAGCCTCTCTGGCAGGTGGGCAAACCGAGGCATGGAGGTTTGTTTAAGGTGAACTGCCAGTGTGTGACCA
        BglI      BspMI-                                                  Dr
                                                                          Pfl
           2035      2045      2055      2065      2075      2085      2095
CCTAGTGGGGTAGAGCTGATGATTGCCTCACACCGGAGCTCCTTCCTGTGCCGCGTTCTGTCCAGAAGACACAGC
aIII                                 SacI                                  N
MI
           2110      2120      2130      2140      2150      2160      2170
CATGGATGTCCATTTTAGGATCAGCCAAGCCCCGTCTTGTCCTTCATTTTTATTTATGTTTTTTTAGAAATGGG
coI
           2185      2195      2205      2215      2225      2235      2245
GTCTTGCTCTGTCACCCAGGCTGGGTGCAGTGGTGTGATCATAGCTCACCGCAGCTTTGACGCCGTCTTCCCACT
                                                             Tth111I
           2260      2270      2280      2290      2300      2310      2320
CAGTCTACTAAGCTTGGACTATAGGCCAAGACTATAGAGTGGTCCTTCTTTCCATTCTTTTGGGACCATGAGAGG
         HindIII                                         BstXI
           2335      2345      2355      2365      2375      2385      2395
CCACCCATGTTTCCTGCCCCTGCTGGGCCCTGCTGCTCAGAAGGCATGGTCTGAGGCTTTCACCTTGGTCGTGAG
                          ApaI
                          EcoO
           2410      2420      2430      2440      2450      2460      2470
CCTTCGTGGTGGTTTCTTTCAGCATGGGGTTGGGATGCTGTGCTCAGGCTTCTGCATGGTTTCCCACACTCTCTT
           2485      2495      2505      2515      2525      2535      2545
CTCCTCCTCAGGACTGGATCATCGCGCCTGAAGGCTACGCGCGCTACTACTGTGAGGGGGAGTGTGCCTTCCCTC
     MstII                                BssHII
           2560      2570      2580      2590      2600      2610      2620
TGAACTCCTACATGAACGCCACCAACCACGCCATCGTGCAGACGCTGGTGGGTGTCACGCCATCTTGGGGTGTGG
                                                                          Bs
           2635      2645      2655      2665      2675      2685      2695
TCACCTGGGCCGGGCAGGCTGCGGGGCCACCAGATCCTGCTGCCTCCAAGCTGGGGCCTGAGTAGATGTCAGCCC
tEII    BglI                                              EcoO
```

Title: OSTEOGENIC DEVICES
Inventor(s): Oppermann et al.
Serial No. 09/754,831
Atty Docket No. STK-008CN
Atty/Agent: Patrick R.H. Waller/kkh
Express Mail Label No. EL902309562US


```
    2710      2720      2730      2740      2750      2760      2770
ATTGCCATGTCATGACTTTTGGGGGCCCCTTGCGCCGTTAAAAAAAAATCAAAAATTGTACTTTATGACTGGTTT
                      ApaI
                     EcoO
    2785      2795      2805      2815      2825      2835      2845
GGTATAAAGAGGAGTATAATCTTCGACCCTGGAGTTCATTTTATTTCTCCTAATTTTTAAAGTAACTAAAAGTTGT
                                                     DraI
    2860      2870      2880      2890      2900      2910      2920
ATGGGCTCCTTTGAGGATGCTTGTAGTATTGTGGGTGCTGGTTACGGTGCCTAAGAGCACTGGGCCCCTGCTTCA
                                                             ApaI
                                                             EcoO
    2935      2945      2955      2965      2975      2985      2995
TTTTCCAGTAGAGGAAACAGGTAAACAGATGAGAAATTTCAGTGAGGGCACAGTGATCAGAAGCGGGCCAGCAG
    3010      3020      3030      3040      3050      3060      3070
GATAATGGGATGGAGAGATGAGTGGGGACCCATGGCCATTTCAAGTTAAATTTCAGTCGGTCACCAGGAAGAT
                        EcoO NcoI                            BstEII
    3085      3095      3105      3115      3125      3135      3145
TCCATGTGATAATGAGATTAACGTGCCCAGTCACGGCGACACTCAGTAGGTGTTATTCCTGCTCTGCCAACAGCA
    3160      3170      3180      3190      3200      3210      3220
ACCATAGTTGATAAGAGCTGTTAGGGATTTTGTCCTTTTGCTTAGAATCCAAGGTTCAAGGACCTTGGTTATGTA
                                                            EcoO
    3235      3245      3255      3265      3275      3285      3295
GCTCCCTGTCATGAACATCATCTGAGCCTTTCCTGCCTACTGATCATCCACCCTGCCTTGAATGCTTCTAGTGAC
                                                             BsmI+
    3310      3320      3330      3340      3350      3360      3370
AGAGAGCTCACTACCAGGACTACTCCCTCCTTTCATTTAGTAATCTGCCTCCTTCTTTTCTTGTCCCTGTCCTGT
  SacI
    3385      3395      3405      3415      3425      3435      3445
GTGTTAAGTCCTGGAGAAAAATCTCATCTATCCCTTTCATTTGATTCTGCTCTTTGAGGGCAGGGGTTTTTGTTT
    3460      3470      3480      3490      3500      3510      3520
CTTTGTTTGTTTTTTTAAGTGTTGGTTTTCCAAAGCCCTTGCTCCCCTCCTCAATTGAAACTTCAAAGCCCTCAT
    3535      3545      3555      3565      3575      3585      3595
TGGGATTGAAGGTCCTTAGGCTGGAAACAGAAGAGTCCTCCCCAACCTGTTCCCTGGCCTGGATGTGCTGTGCTG
       EcoOMstII
```

Fig. 1A-4

```
          3610      3620      3630      3640      3650      3660      3670
TGCCAGTATCCCCTGGAAGGTGCCAGGCATGTCTCCCCGGCTGCCAGGGGACACATCTCTATCCTTCTCCAACCC
          3685      3695      3705      3715      3725      3735      3745
CTGCCTTCATGGCCCATGGAACAGGAGTGCCATCGCCCTGTGTGCACCTACTTCCATCAGTATTTCACCAGAGAT
  BglI        NcoI                          ApaLI                        BglI
           3760      3770      3780      3790      3800      3810      3820
CTGCAGGATCAAAGTGAATTCTCCAGGGATTGTGAAATGATGCGATTGTGGTCATGTTTAAAAGGGGGCAACTGT
I               EcoRI                                       DraI
PstI
          3835      3845      3855      3865      3875      3885      3895
CTTCTAGAGAGTCCTGATGAAATGCTTCCAGAGGAAATGAGCTGATGGCTGGAATTTGCTTTAAAATCATTCAAG
  XbaI                                                        DraI
          3910      3920      3930      3940      3950      3960      3970
GTGGAGCAGGTGGGGAAGGGTATGGATGTGTAAGAGTTTGAAATTGTCCATCATAAAATGTGTAAAAAGCATGCT
     BspMI-                                                           SphI
          3985      3995      4005      4015      4025      4035      4045
GGCCTATGTCAGCAGTCACAGCCTGGAGGTGGTAACAGAGTGCCAGTCACTGATGCTCAAGCCTGGCACCTACAG
          4060      4070      4080      4090      4100      4110      4120
TTGCTGGAAACCCAGAAGTTTCACGTTGAAAACAACAGGACAGTGGAATCTCTGGCCCTGTCTTGAACACGTGGC
          4135      4145      4155      4165      4175      4185      4195
AGATCTGCTAACACTGATCTTGGTTGGCTGCCGTCAGCTTAGGTTGAGTGGCGGTCTTCCCTTAGTTTGCTTAGT
BglII
          4210      4220      4230      4240      4250      4260      4270
CCCCGCTATTCCCTATTGTCTTACCTCGGTCTATTTTGCTTATCAGTGGACCTCACGAGGCACTCATAGGCATTT
          4285      4295      4305      4315      4325      4335      4345
GAGTCTATGTGTCCCTGTCCCACATCCTCTGTAAGGTGCAGAGAAGTCCATGAGCAAGATGGAGCACTTCTAGTG
          4360      4370      4380      4390      4400      4410      4420
GGTCCAAGTCAGGGACACTATTCAGCAATCTACAGTGCACAGGGCAGTTCCCCAACAGAGAATTACCTGGTCCTG
                                  ApaLI
          4435      4445      4455      4465      4475      4485      4495
AATGTCGGATCTGGCCCCTTCCTTCCCCACTGTATAATGTGAAAACCTCTATGCTTTGTTCCCCTTGTCTGCAAA
          4510      4520      4530      4540      4550      4560      4570
ACAGGGATAATCCCAGAACTGAGTTGTCCATGTAAAGTGCTTAGAACAGGGAGTGCTTGGCTTGGGGAGTGTCAC
                                                                          Bs
```

Fig. 1A-5

```
        4585      4595      4605      4615      4625      4635      4645
CTGCAGTCATTCATTATGCCCAGACAGGATGTTTCTTTATAGAAACGTGGAGGCCAGTTAGAACGACTCACCGCT
pMI+
PstI
        4660      4670      4680      4690      4700      4710      4720
TCTCACCACTGCCCATGTTTTGGTGTGTGTTTCAGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCT
            PflMI
        4735      4745      4755      4765      4775      4785      4795
GTGCGCCCACGCAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACA
        4810      4820      4830      4840
GAAACATGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCTCCGA
```

Fig. 1A-6

Title: OSTEOGENIC DEVICES
Inventor(s): Oppermann et al.
Serial No. 09/754,831
Atty Docket No. STK-008CN
Atty/Agent: Patrick R.H. Waller/kkh
Express Mail Label No. EL902309562US


```
CONSENSUS  PROBE   20        30        40        50        60        70
GATCCTAATGGGCTGTACGTGGACTTCCAGCGCGACGTGGGCTGGGACGACTGGATCATCGCCCCCGTCG
       **                         ** *** ********  ************** **
TGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACTGGATCATCGCGCCTGAAG
OP4      28        38        48        58        68        78        88

        80        90       100       110       120       130       140
ACTTCGACGCCTACTACTGCTCCGGAGCCTGCCAGTTCCCCTCTGCGGATCACTTCAACAGCACCAACCA
 ** **     ********* **     **    **    *****           **   ***  *********
GCTACGCGCGCTACTACTGTGAGGGGGAGTGTGCCTTCCCTCTGAACTCCTACATGAACGCCACCAACCA
        98        108       118       128       138       148       158

       150       160       170       180       190       200       210
CGCCGTGGTGCAGACCCTGGTGAACAACATGAACCCCGGCAAGGTACCCAAGCCCTGCTGCGTGCCCACC
****   ******** *****  **  *** *****         *** *************    ******
CGCCATCGTGCAGACGCTGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACG
       168       178       188       198       208       218       228

       220       230       240       250       260       270       280
GAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATTCCACCGTGGTGCTGAAGAACTACCAGGAGA
 ****    ******        ** ***   ** **   **** ***   ******** ***        *
CAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGAAACA
       238       248       258       268       278       288       298

       290       300       310
TGACCGTGGTGGGCTGCGGCTGCCGCTAACTGCA
**    **   ** *** ******** *** **
TGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCT
       308       318       328
```

Fig. 1B

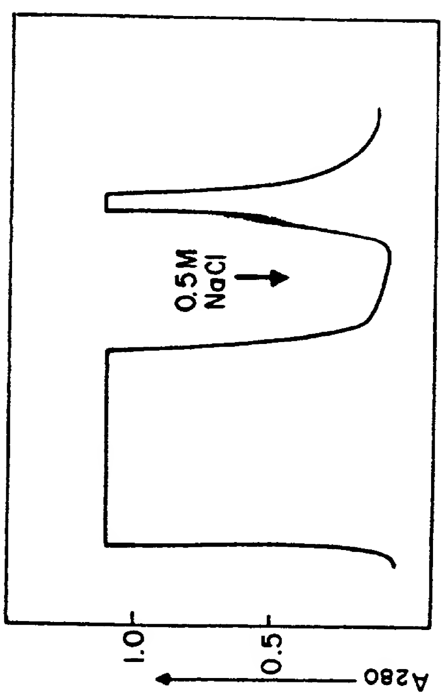

Fig. 2A

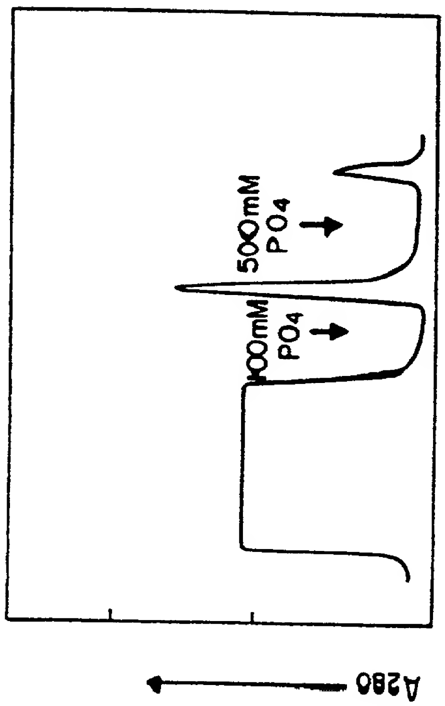

Fig. 2B

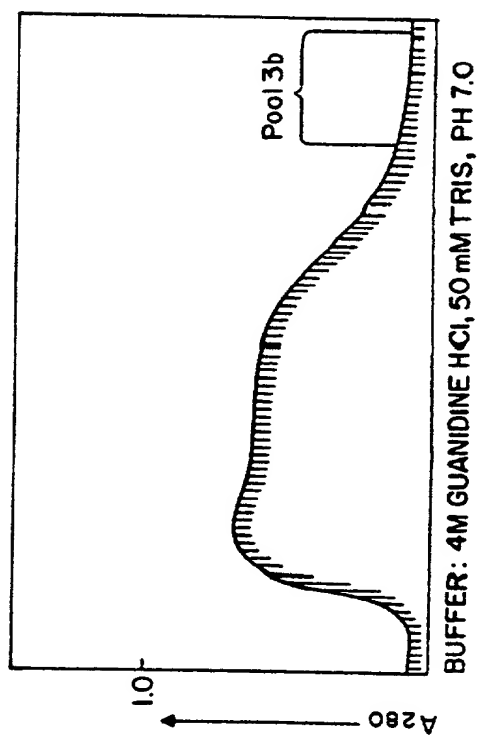

Fig. 2C

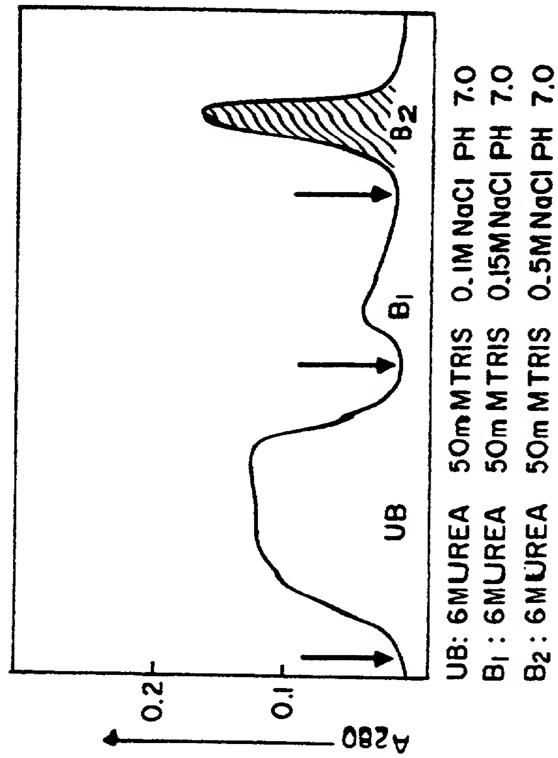

Fig. 2D

Fig. 3A

Fig. 3B

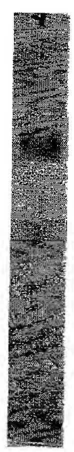

Fig. 4A

Fig. 4B

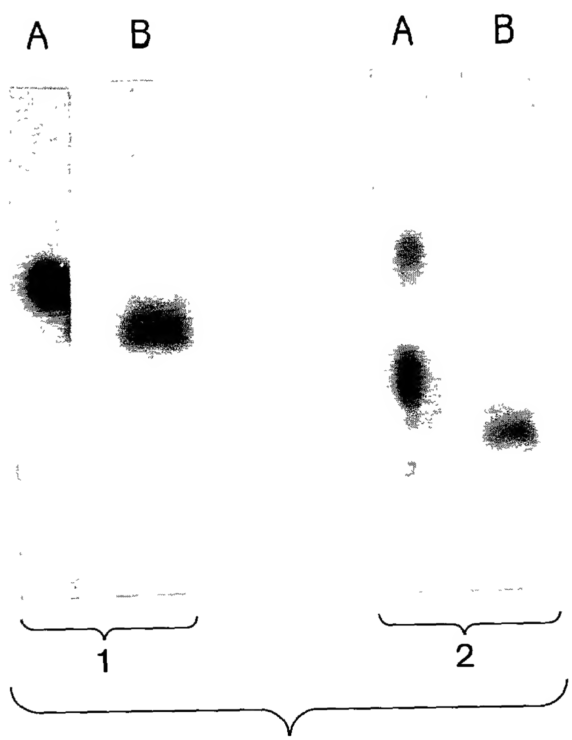

Fig. 5

Fig. 6E

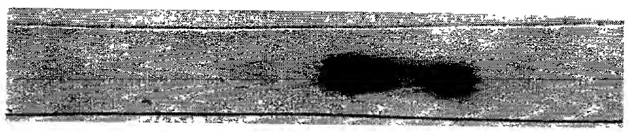

Fig. 6D

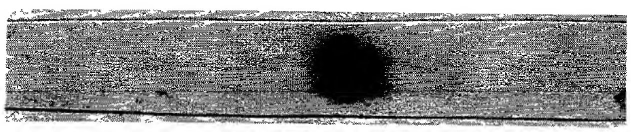

Fig. 6C

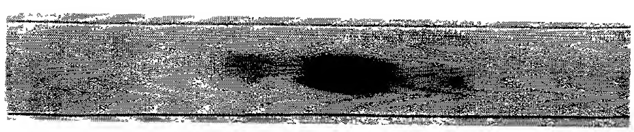

Fig. 6B

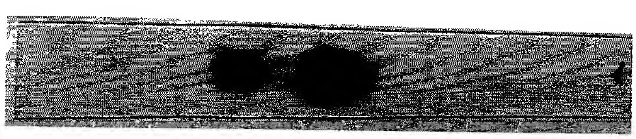

Fig. 6A

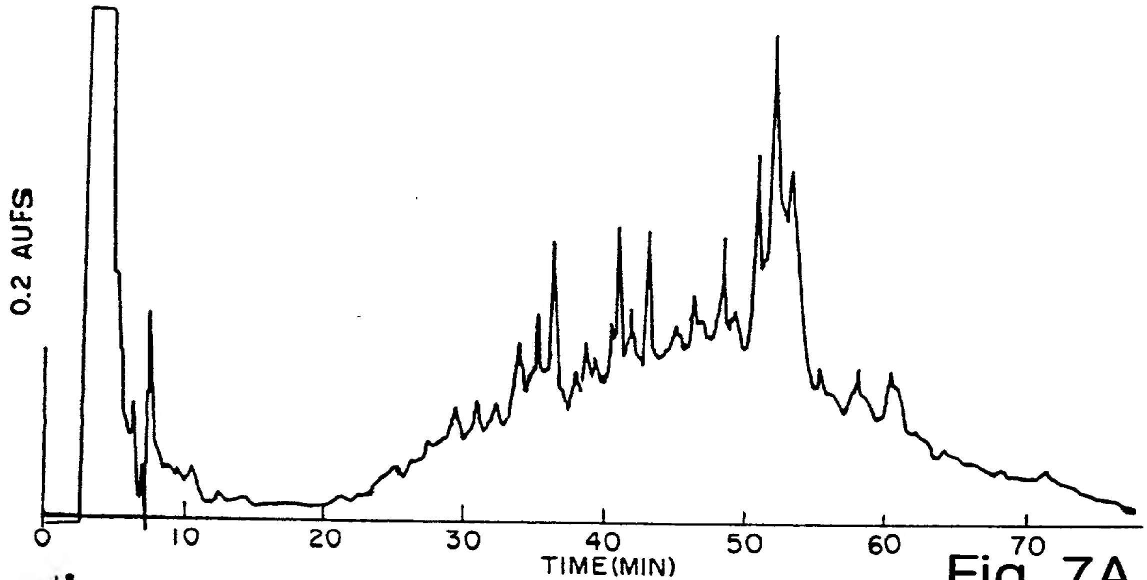

Fig. 7A

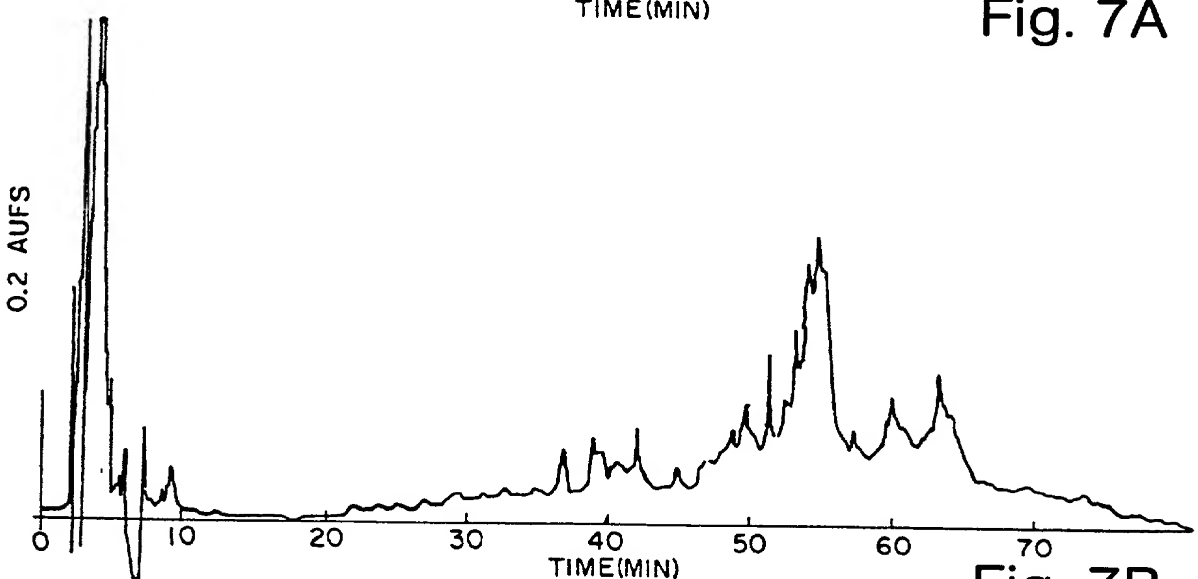

Fig. 7B

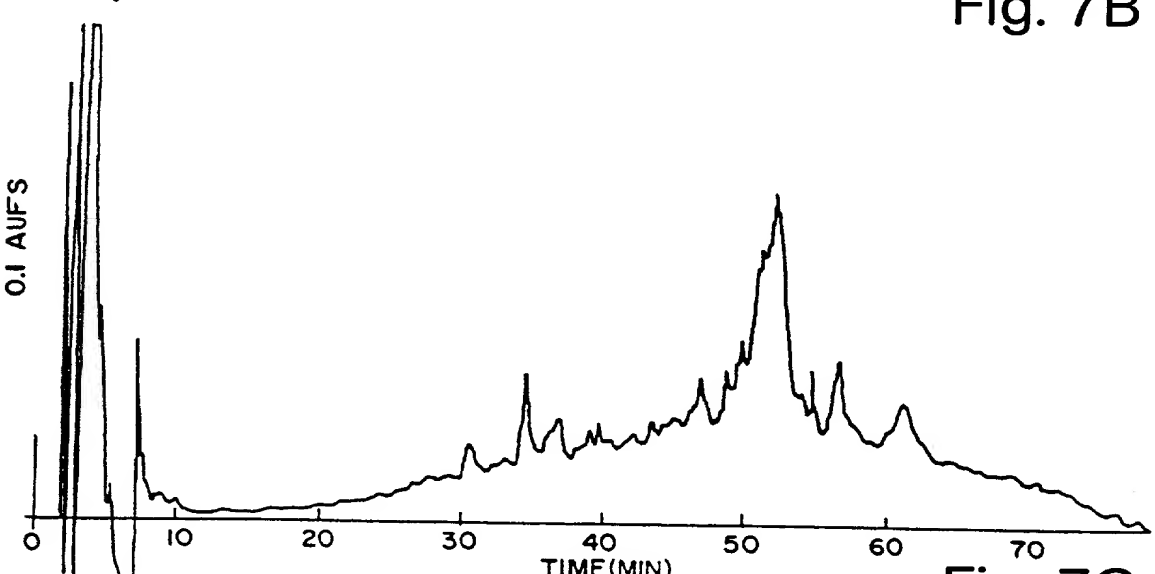

Fig. 7C

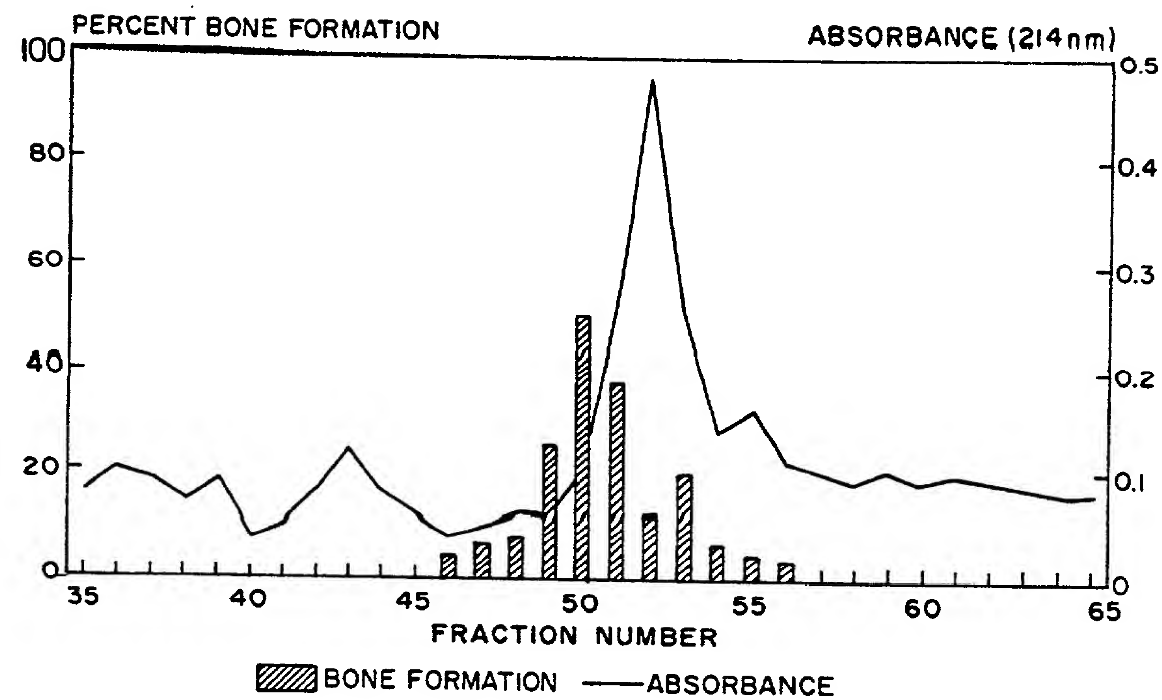
PERCENT BONE FORMATION
ABSORBANCE (214nm)
100
80
60
40
20
0
0.5
0.4
0.3
0.2
0.1
0
35
40
45
50
55
60
65
FRACTION NUMBER
BONE FORMATION
ABSORBANCE

Fig. 8

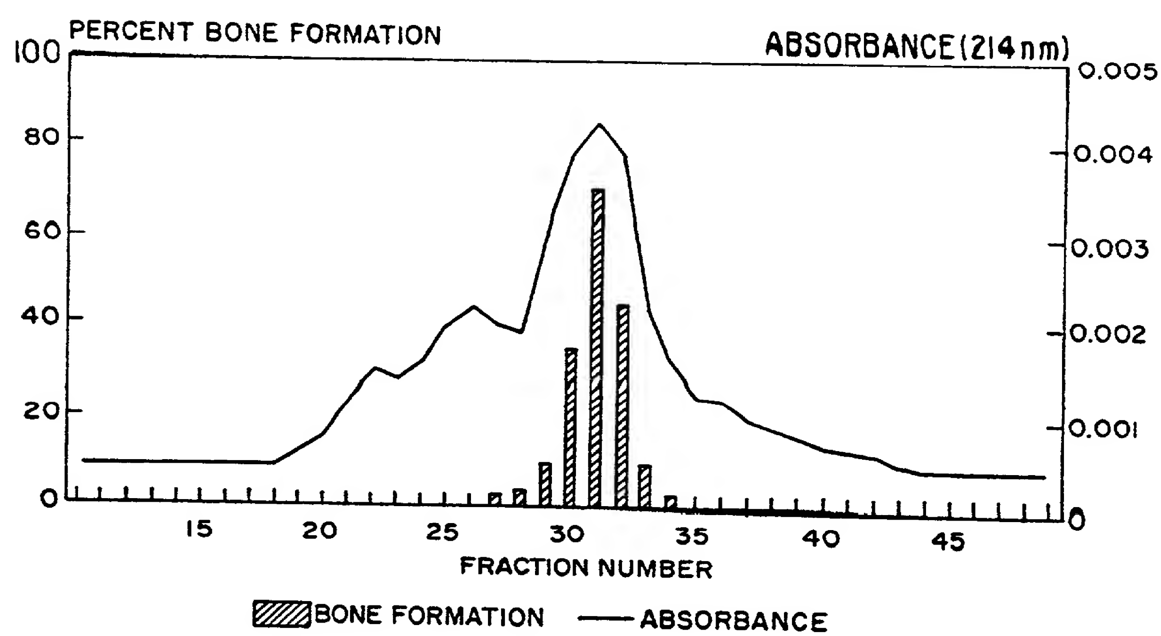
PERCENT BONE FORMATION
ABSORBANCE (214nm)
100
80
60
40
20
0
0.005
0.004
0.003
0.002
0.001
0
15
20
25
30
35
40
45
FRACTION NUMBER
BONE FORMATION
ABSORBANCE

Fig. 9

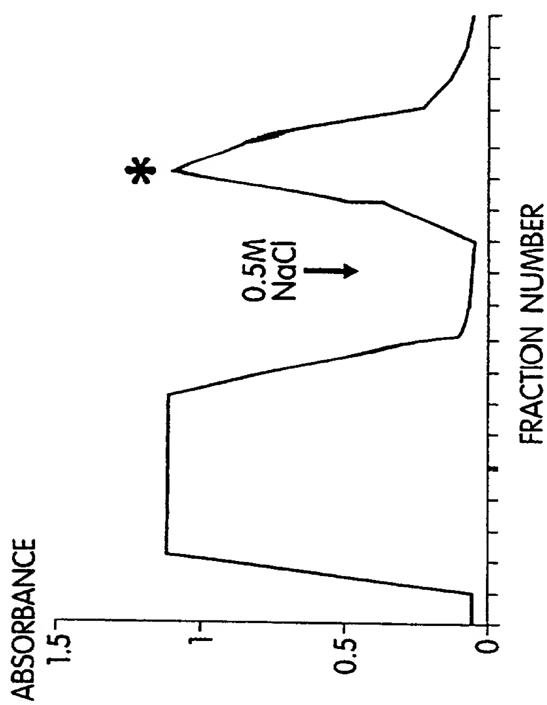

Fig. 10A

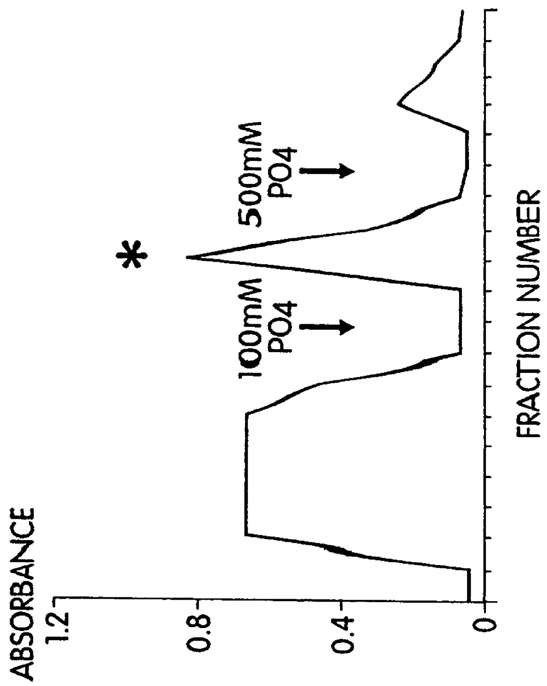

Fig. 10B

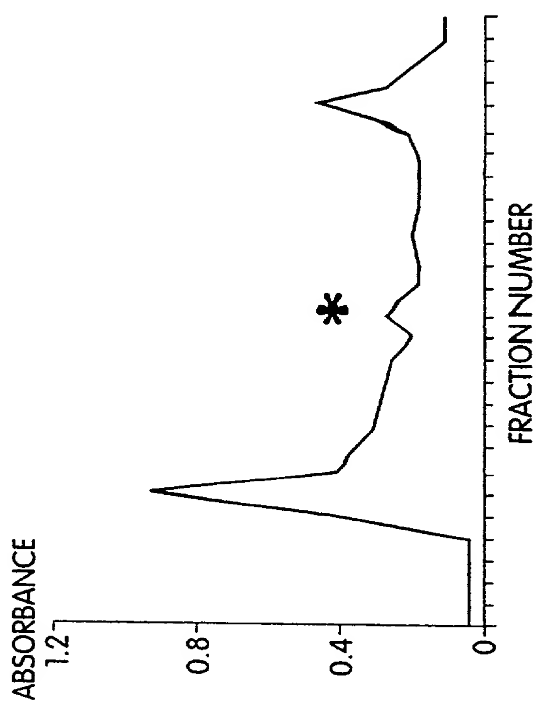

Fig. 10C

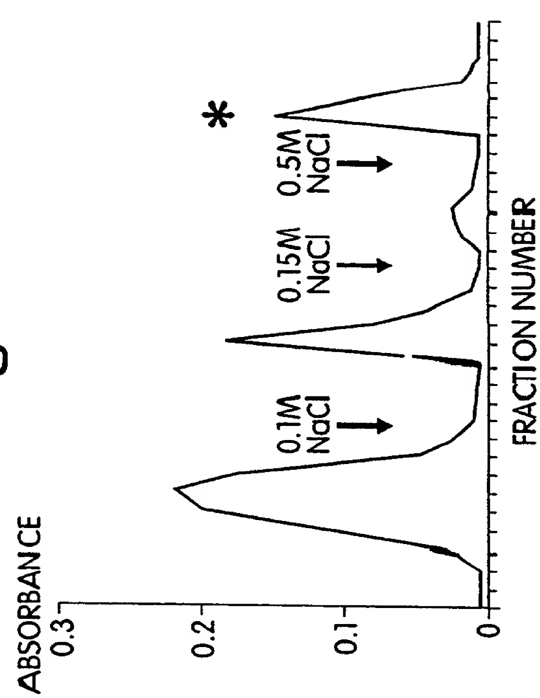

Fig. 10D

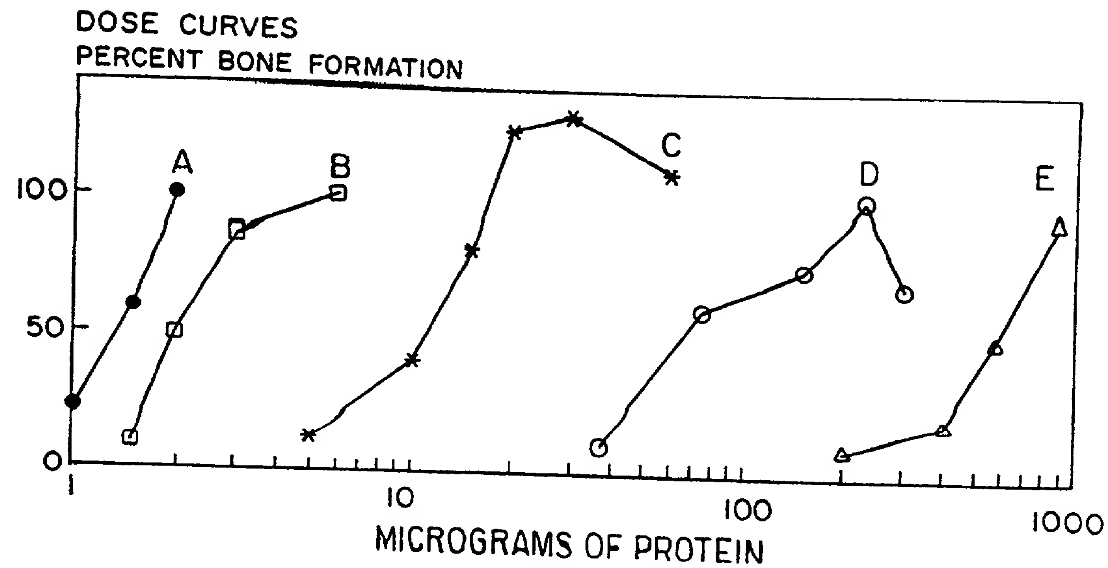
DOSE CURVES
PERCENT BONE FORMATION
A
B
C
D
E
100
50
0
1
10
100
1000
MICROGRAMS OF PROTEIN

Fig. 11

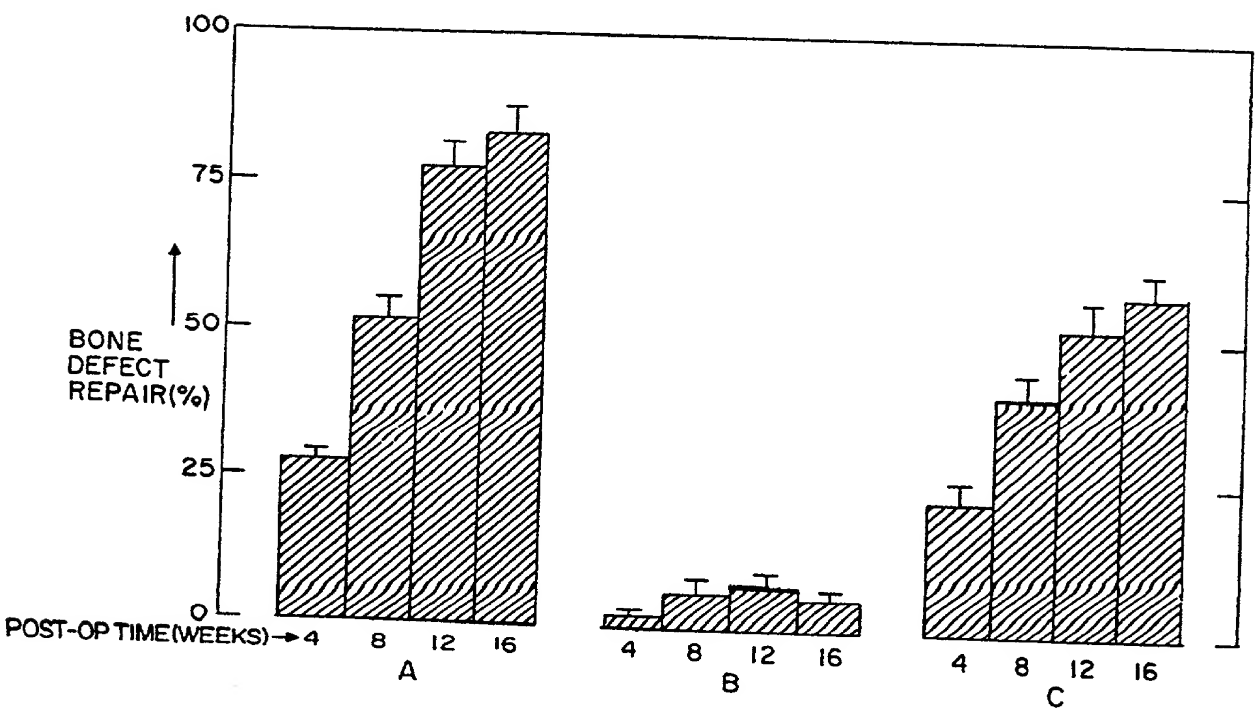
100
75
50
25
0
BONE DEFECT REPAIR(%)
POST-OP TIME(WEEKS)→ 4
8
12
16
A
4
8
12
16
B
4
8
12
16
C

Fig. 12

Title: OSTEOGENIC DEVICES
Inventor(s): Oppermann et al.
Serial No. 09/754,831
Atty Docket No. STK-008CN
Atty/Agent: Patrick R.H. Waller/kkh
Express Mail Label No. EL902309562US


```
          10        20        30        40        50
GATCCTAATGGGCTGTACGTGGACTTCCAGCGCGACGTGGGCTGGGACGA
 D  P  N  G  L  Y  V  D  F  Q  R  D  V  G  W  D  D

          60        70        80        90       100
CTGGATCATCGCCCCCGTCGACTTCGACGCCTACTACTGCTCCGGAGCCT
  W  I  I  A  P  V  D  F  D  A  Y  Y  C  S  G  A

         110       120       130       140       150
GCCAGTTCCCCTCTGCGGATCAATTCAACAGCACCAACCACGCCGTGGTG
C  Q  F  P  S  A  D  H  F  N  S  T  N  H  A  V  V

         160       170       180       190       200
CAGACCCTGGTGAACAACATGAACCCCGGCAAGGTACCCAAGCCCTGCTG
 Q  T  L  V  N  N  M  N  P  G  K  V  P  K  P  C  C

         210       220       230       240       250
CGTGCCCACCGAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATT
  V  P  T  E  L  S  A  I  S  M  L  Y  L  D  E  N

         260       270       280       290       300
CCACCGTGGTGCTGAAGAACTACCAGGAGATGACCGTGGTGGGCTGCGGC
S  T  V  V  L  K  N  Y  Q  E  M  T  V  V  G  C  G

         310
TGCCGCTAACTGCAG
 C  R  *
```

Fig. 13

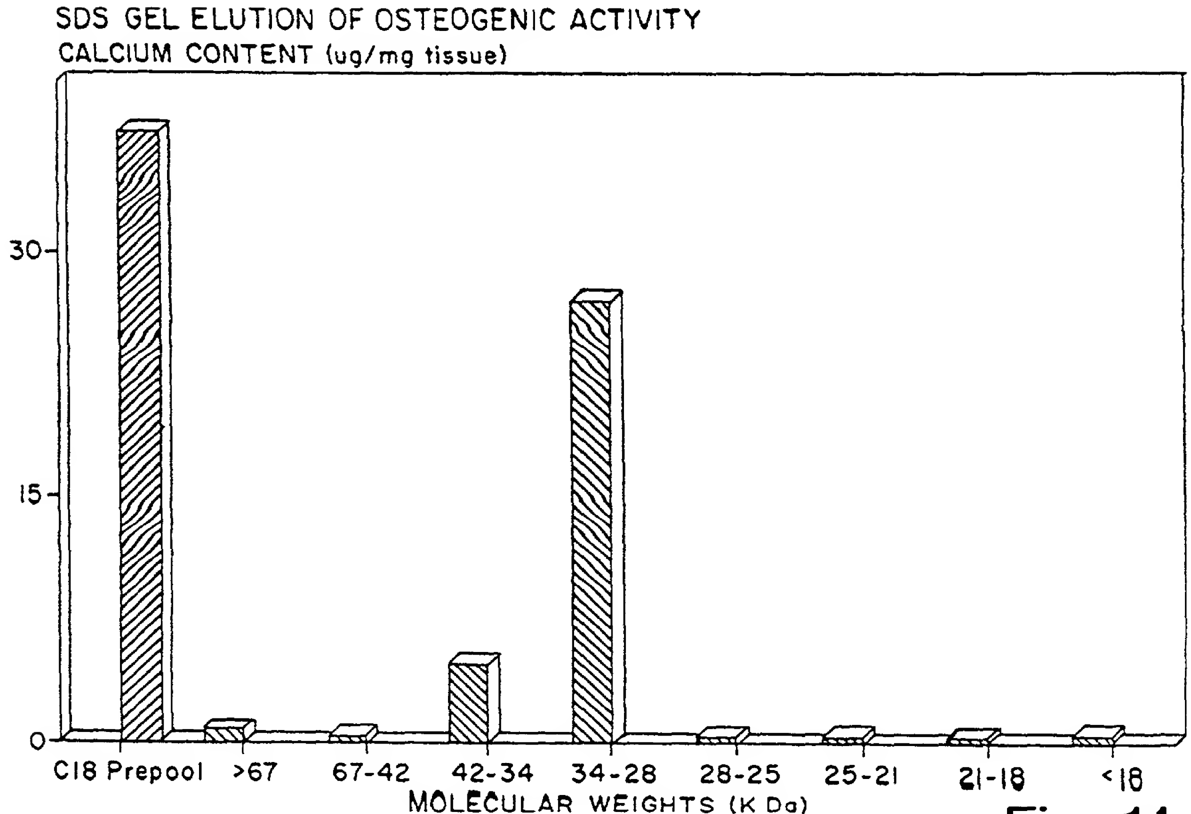
SDS GEL ELUTION OF OSTEOGENIC ACTIVITY
CALCIUM CONTENT (ug/mg tissue)
30
15
0
C18 Prepool
>67
67-42
42-34
34-28
28-25
25-21
21-18
<18
MOLECULAR WEIGHTS (K Da)

Fig. 14

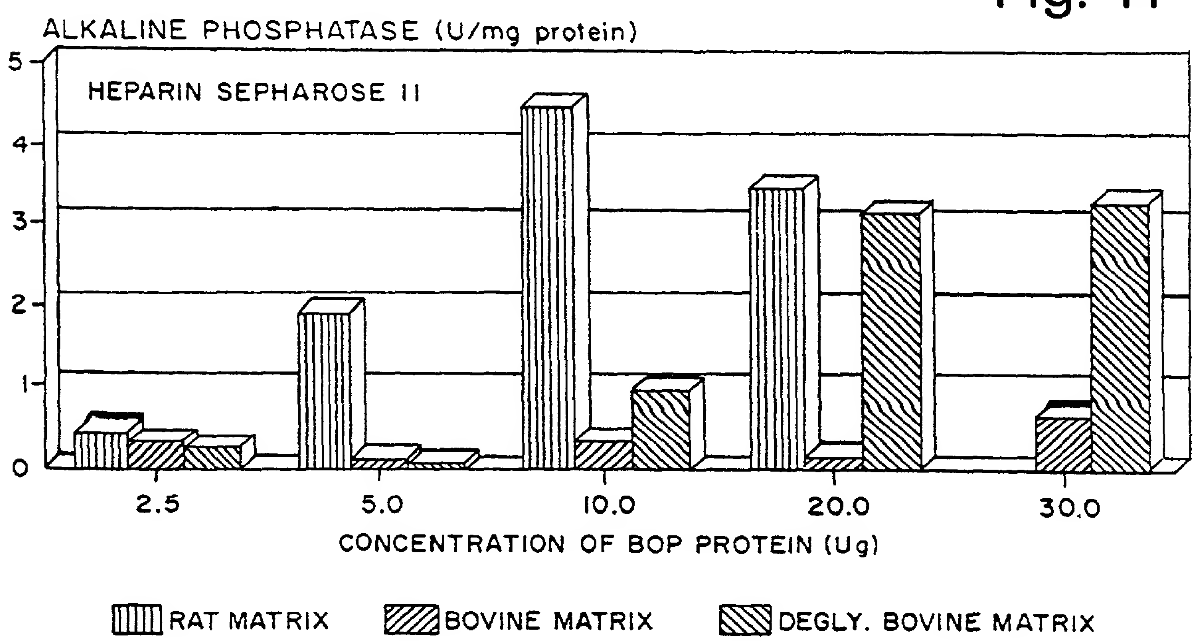
ALKALINE PHOSPHATASE (U/mg protein)
HEPARIN SEPHAROSE II
5
4
3
2
1
0
2.5
5.0
10.0
20.0
30.0
CONCENTRATION OF BOP PROTEIN (Ug)
RAT MATRIX
BOVINE MATRIX
DEGLY. BOVINE MATRIX

Fig. 19

Title: OSTEOGENIC DEVICES
Inventor(s): Oppermann et al.
Serial No. 09/754,831
Atty Docket No. STK-008CN
Atty/Agent: Patrick R.H. Waller/kkh
Express Mail Label No. EL902309562US

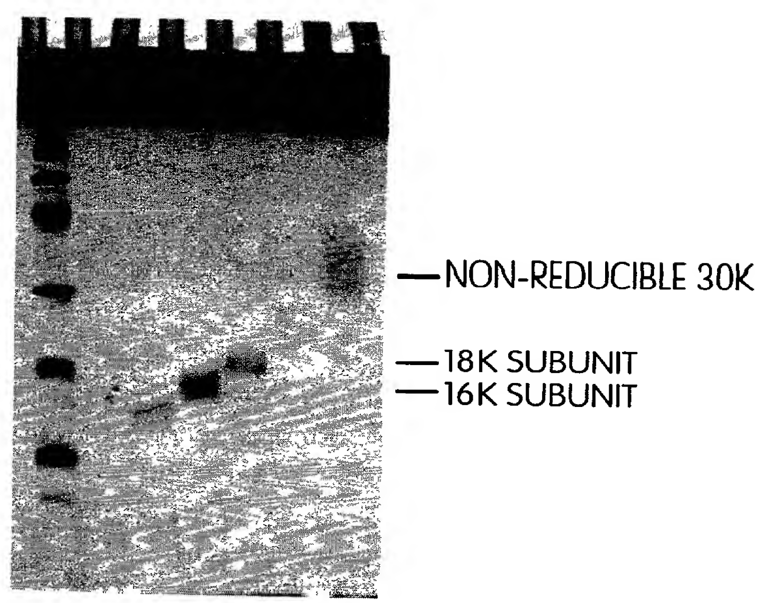

Fig. 15

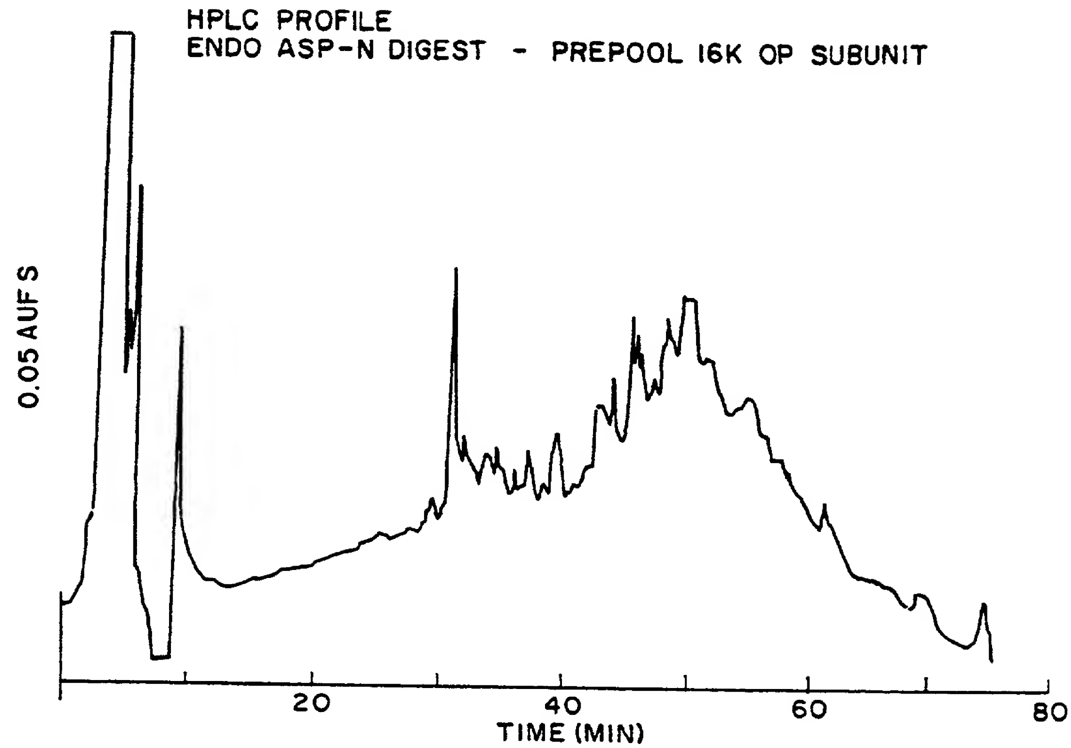

Fig. 16A

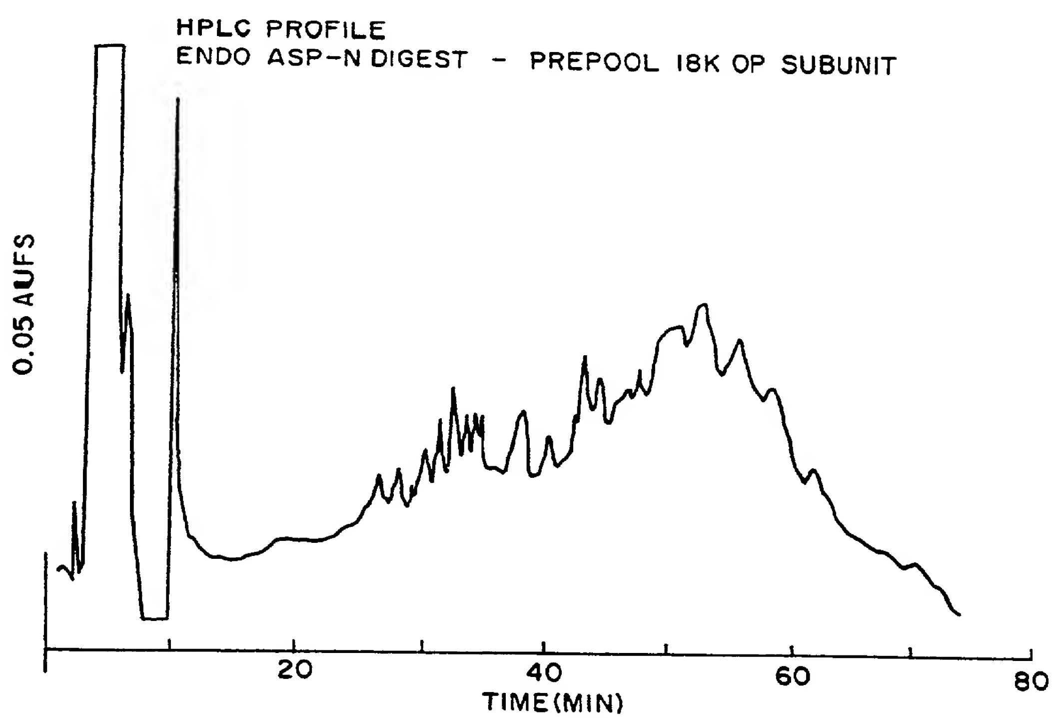

Fig. 16B

Fig. 17A

Fig. 17B

Fig. 17C

Title: OSTEOGENIC DEVICES
Inventor(s): Oppermann et al.
Serial No. 09/754,831
Atty Docket No. STK-008CN
Atty/Agent: Patrick R.H. Waller/kkh
Express Mail Label No. EL902309562US

COP1	COP3	COP4	COP5	COP7	VG1	DPP	OP1	CBMP2 a)	CBMP2 b)	CBMP3 (bov)	beta-Inhibin a)	beta-Inhibin b)	TGF-beta 1	TGF-beta 2	TGF-beta 3	MIS	alpha-Inhib	consensus choices
					C	C	C	C		C	C	C	C			C	C	c
					K	R	K	K	R	A	C	C	C			A	H	k,r
<P	P	P	P	P>	K	R	K	R		R	K	R	V	L	V	L	R	k,r
<N	N	N	N	N>	R	H	H	H		R	K	Q	R			R	V	h,k,r,q
<G	G	G	G	G>	H	S	E	P	S	Y	Q	Q	Q	P	P	E	A	p,s,e,q
L	L	L	L	L	L	L	L	L		L	F	F	L			L	L	l
Y	Y	Y	Y	Y	Y	Y	Y	Y		K	F	F	Y			S	N	y,f
V	V	V	V	V	V	V	V	V		V	V	I	I			V	I	v,i
D	D	D	D	D	E	D	S	D		D	S	D	D			D	S	d,e,s
F	F	F	F	F	F	F	F	F		F	F	F	F			L	F	f
Q	Q	S	S	S	K	S	R	S		A	K	R	R	K	R	R	Q	k,r,s
R	R												K	R	Q	A		
D	D	D	D	D	D	D	D	D		D	D		D			E	E	d
V	V	V	V	V	V	V	L	V		I	I	I	L			R	L	v,l,i
G	G	G	G	G	G	G	G	G		G	G	G	G			S	G	g
W	W	W	W	W	W	W	W	W		W	W	W	W				W	w
D	D	D	D	N	Q	D	Q	N		S	N	N	K				E	q,n,d,e,s
D	D	D	D	D	N	D	D	D		E	D	D	-				R	d,e,n
W	W	W	W	W	W	W	W	W		W	W	W	W				W	w
I	I	I	I	I	V	I	I	I		I	I	I	I	I	V	V	I	i,v
I	V	V	V	V	I	V	I	V		I	I	I	H			L	V	i,v
A	A	A	A	A	A	A	A	A		S	A	A	E			I	Y	a,s
P	P	P	P	P	P	P	P	P		P	P	P	P			P	P	p
V	P	P	P	P	Q	L	E	P		K	S	T	K			E	P	e,q,p*
D	G	G	G	G	G	G	G	G		S	G	G	G			T	S	g,s
F	Y	Y	Y	Y	Y	Y	Y	Y		F	Y	Y	Y			Y	F	y,f
D	Q	Q	Q	H	M	D	A	H		D	H	Y	H	N	Y	Q	I	h,d,n,q,y*
A	A	A	A	A	A	A	A	A		A	A	G	A			A	F	a

Fig. 18-1

Y	F	F	F	F	::	N	Y	Y	F	:	Y	N	N	N			:	N	H	::	y,f,n
Y	Y	Y	Y	Y	::	Y	Y	Y	Y	:	Y	Y	Y	F			:	N	Y	::	y,f,n
C	C	C	C	C	::	C	C	C	C	:	C	C	C	C			:	C	C	::	c
S	S	S	H	H	::	Y	H	E	H	:	S	E	E	L	A	S	:	Q	H	::	e,h,*
G	G	G	G	G	::	G	G	G	G	:	G	G	G	G			:	G	G	::	g
A	A	A	E	E	::	E	K	E	E	:	A	E	S	P	A	P	:	V	G	::	e,a*
C	C	C	C	C	::	C	C	C	C	:	C	C	C	C			:	C	C	::	c
Q	Q	Q	P	P	::	P	P	A	P	:	Q	P	P	P			:	G	G	::	p,a,g,q
F	F	F	F	F	::	Y	F	F	F	:	F	S	A	Y			:	W	L	::	f,y
P	P	P	P	P	::	P	P	P	P	:	P	H	Y	I	L	L	:	P	H	::	p
S	S	S	L	L	::	L	L	L	L	:	M	I	L	W	W	R	:	Q	I	::	l,m,i
A	A	A	A	A	::	T	A	N	A	:	P	A	A	S			:	S	P	::	p,a,s,t
D	D	D	D	D	::	E	D	S	D	:	K	G	G				:	D	P	::	d,e,s,g*
H	H	H	H	H	::	I	H	Y	H	:	S	T	V	L			:	R	N	::	h,r,n, s*
F	F	F	F	L	::	L	F	M	L	:	L	S	P	L	S	A	:		L	::	m,l,f,p,sa
N	N	N	N	N	::	N	N	N	N	:	K	G	G	D			:	N	S	::	n,k
S	S	S	S	S	::	G	S	A	S	:	P	S	S				:	P	L	::	s,a,p,g
T	T	T	T	T	::	S	T	T	T	:	S	S	A	T			:	R	P	::	t,s,a
N	N	N	N	N	::	N	N	N	N	:	N	L	S	Q	Q	T	:	Y	V	::	n
					::					:		S	S				:	G	P	::	
					::					:		F	F				:	N	G	::	
H	H	H	H	H	::	H	H	H	H	:	H	H	H	Y	H	H	:	H	A	::	h
					::					:		S	T				:			::	
A	A	A	A	A	::	A	A	A	A	:	A	T	A	S			:		P	::	a,t,s
V	V	V	V	V	::	I	V	I	I	:	T	V	V	K	R	T	:	V	P	::	i,v,t
V	V	V	V	V	::	L	V	V	V	:	I	I	V	V			:	V	T	::	v,i,l
Q	Q	Q	Q	Q	::	Q	Q	Q	Q	:	Q	N	N	L			:	L	P	::	q,n
T	T	T	T	T	::	T	T	T	T	:	S	H	Q	A	S	G	:	L	A	::	t, s,a,g
L	L	L	L	L	::	L	L	L	L	:	I	Y	Y	L			:	L	Q	::	l,i
V	V	V	V	V	::	V	V	V	V	:	V	R	R	Y			:	K	P	::	v
N	N	N	N	N	::	H	N	H	N	:	R	M	M	N			:	M	Y	::	h,n r

Fig. 18-2

N	N	N	S	S	::	S	N	F	S		:	A	R	R	Q	T	T:	Q	S	:: n,s *
M	M	M	V	V	::	I	N	I	V		:	V	G	G	H	I	L:	A	L	:: i,v,l,
N	N	N	N	N	::	E	N	N	N		:	G	H	L	N		:	R	L	:: n
					::						:	V	S	N			:	G		::
					::						:	V					:	A		::
P	P	P	S	S	::	P	P	P	S		:	P	P	P	P		:	A	P	:: p,s,a
G	G	G			::	E	G	E			:	G	F	G	G	E	E:	L	G	:: g,e
					::						:		A	T	A		:	A		::
K	K	K	K	K	::	Q	K	T	K	S	:		N	K	S		:	R		:: k,q,t,s
V	V	V	I	I	::	I	V	V	I		:	I	L	V	A		:			:: i,v,l
P	P	P	P	P	::	P	P	P	P		:	P			A	S	S:	P	A	:: p,a,s
K	K	K	K	K	::	L	K	K	K		:	E	K	N			:		Q	:: k
P	P	P	A	A	::	P	A	A	A		:	P	S	S	P		:	P	P	:: a,p,s
C	C	C	C	C	::	C	C	C	C		:	C	C	C	C		:	C	C	:: c
C	C	C	C	C	::	C	C	C	C		:	C	C	C	C		:	C	C	:: c
V	V	V	V	V	::	V	V	A	V		:	V	V	I	V		:	V	A	:: v,a,i
P	P	P	P	P	::	P	P	P	P		:	P	P	P	P	S	P:	P	A	:: p,s,a
T	T	T	T	T	::	T	T	T	T		:	E	T	T	Q		:	T	L	:: t,e,q
E	E	E	E	E	::	K	Q	Q	E		:	K	K	K	A	D	D:	A	P	:: q,e,d,k*
L	L	L	L	L	::	M	L	L	L		:	M	L	L	L		:	Y	G	:: l,m
S	S	S	S	S	::	S	D	N	S		:	S	R	S	E		:	A	T	:: s,n e,d
A	A	A	A	A	::	P	S	A	A		:	S	P	T	P		:	G	M	:: a,s,p,t
I	I	I	I	I	::	I	V	I	I		:	L	M	M	L		:	K	R	:: i,l,m,v
S	S	S	S	S	::	S	A	S	S		:	S	S	S	P	T	T:	L	P	:: s,a,p,t
M	M	M	M	M	::	M	M	V	M		:	I	M	M	I		:	L	L	:: v,m,i,l
L	L	L	L	L	::	L	L	L	L		:	L	L	L	V	L	L:	I	H	:: l,v,i
Y	Y	Y	Y	Y	::	F	Y	Y	Y		:	F	Y	Y	Y		:	S	V	:: y,f
L	L	L	L	L	::	Y	L	F	L		:	F	Y	F	Y		:	L	R	:: f,l,y
D	D	D	D	D	::	D	N	D	D		:	D	D	D	V	I	V:	S	T	:: d,n
E	E	E	E	E	::	N	D	D	E		:	E	D	D	G		:	E	T	:: d,e,
N	N	N	N	N	::	N	Q	S	N	Y	:	N	G	E	R	K	R:	E	S	:: n,q,y*
E	E	E	E	E	::	D	S	S	E	D	:	K	Q	Y	K	T	T:	R	D	:: e,d,s,t

Fig. 18-3

K	K	K	K	K	::	N	T	N	K		:	N	N	N	P			:	I	G	::	n,k
V	V	V	V	V	::	V	V	V	V		:	V	I	I	K			:	S	G	::	v,i
V	V	V	V	V	::	V	V	I	V		:	V	I	V	V	I	V	:	A	Y	::	v,i
L	L	L	L	L	::	L	L	L	L		:	L	K	K	E			:	H	S	::	l
K	K	K	K	K	::	R	K	K	K		:	K	K	R	Q			:	H	F	::	k,r
N	N	N	N	N	::	H	N	K	N		:	V	D	D	L			:	V	K	::	n,d,k*
Y	Y	Y	Y	Y	::	Y	Y	Y	Y		:	Y	I	V				:		Y	::	y
Q	Q	Q	Q	Q	::	E	Q	R	Q		:	P	Q	P	S			:	P	E	::	q,e,p,r
					::						:							:		TVP	::	
E	E	E	E	E	::	N	E	N	D	E	:	N	N	N	N			:	N	N	::	n,d,e
M	M	M	M	M	::	M	M	M	M		:	M	M	M	M			:	M	L	::	m
V	V	V	V	V	::	A	T	V	V		:	T	I	I	I	I	V	:	V	L	::	v,i,t,a
V	V	V	V	V	::	V	V	V	V		:	V	V	V	V			:	A	T	::	v
E	E	E	E	E	::	D	V	R	E		:	E	E	E	R	K	K	:	T	Q	::	e,d,r,k,
G	G	G	G	G	::	E	G	A	G		:	S	E	E	S			:	E	H	::	g,a,s,e
C	C	C	C	C	::	C	C	C	C		:	C	C	C	C			:	C	C	::	c
G	G	G	G	G	::	G	G	G	G		:	H	G	G	K			:	G	A	::	g,h
C	C	C	C	C	::	C	C	C	C		:	C	C	C	C			:	C	C	::	c
R	R	R	R	R	::	R	R	H	R		:	R	S	A	S			:	R	I	::	r,h,s,a,

Fig. 18-4

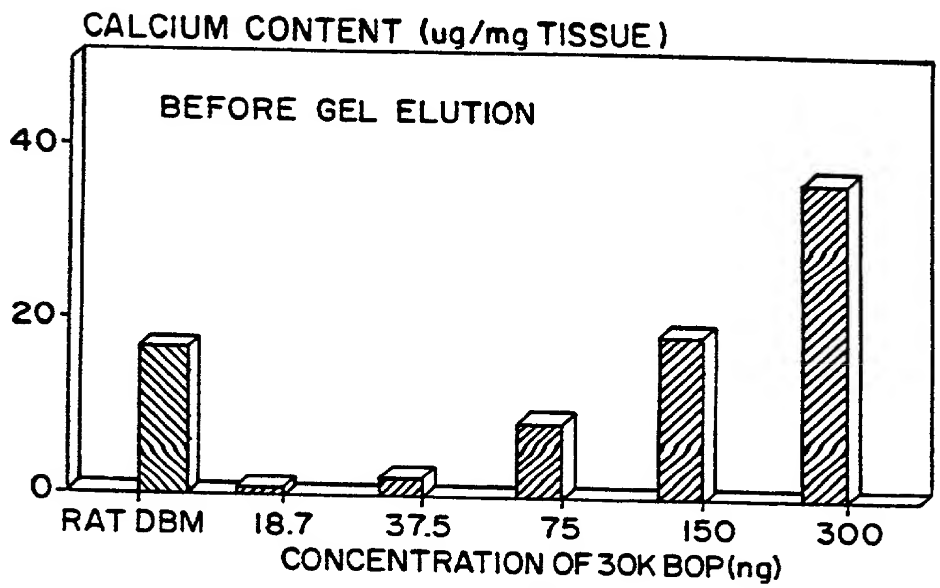

Fig. 20A

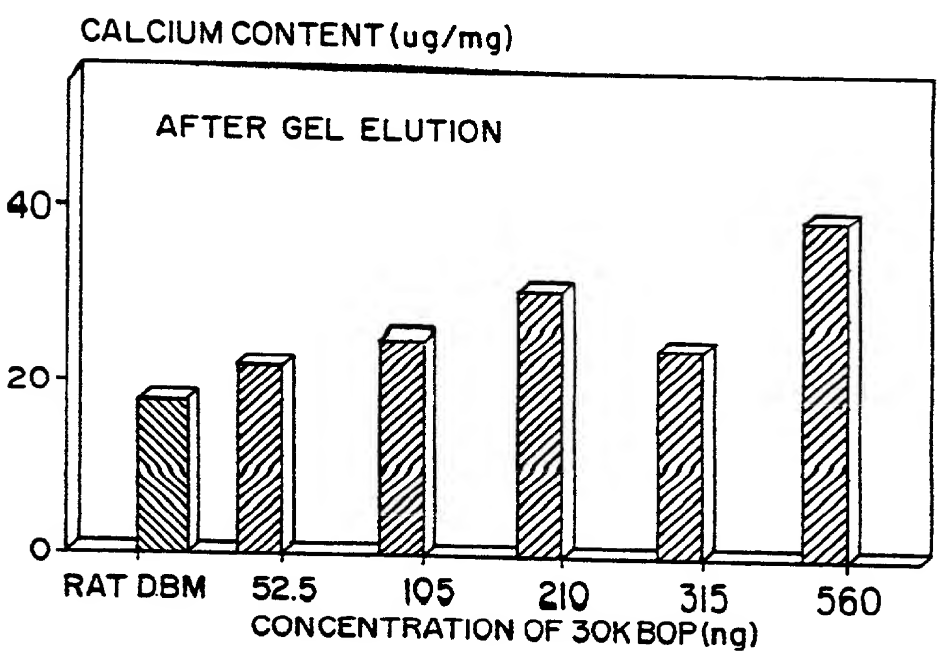

Fig. 20B

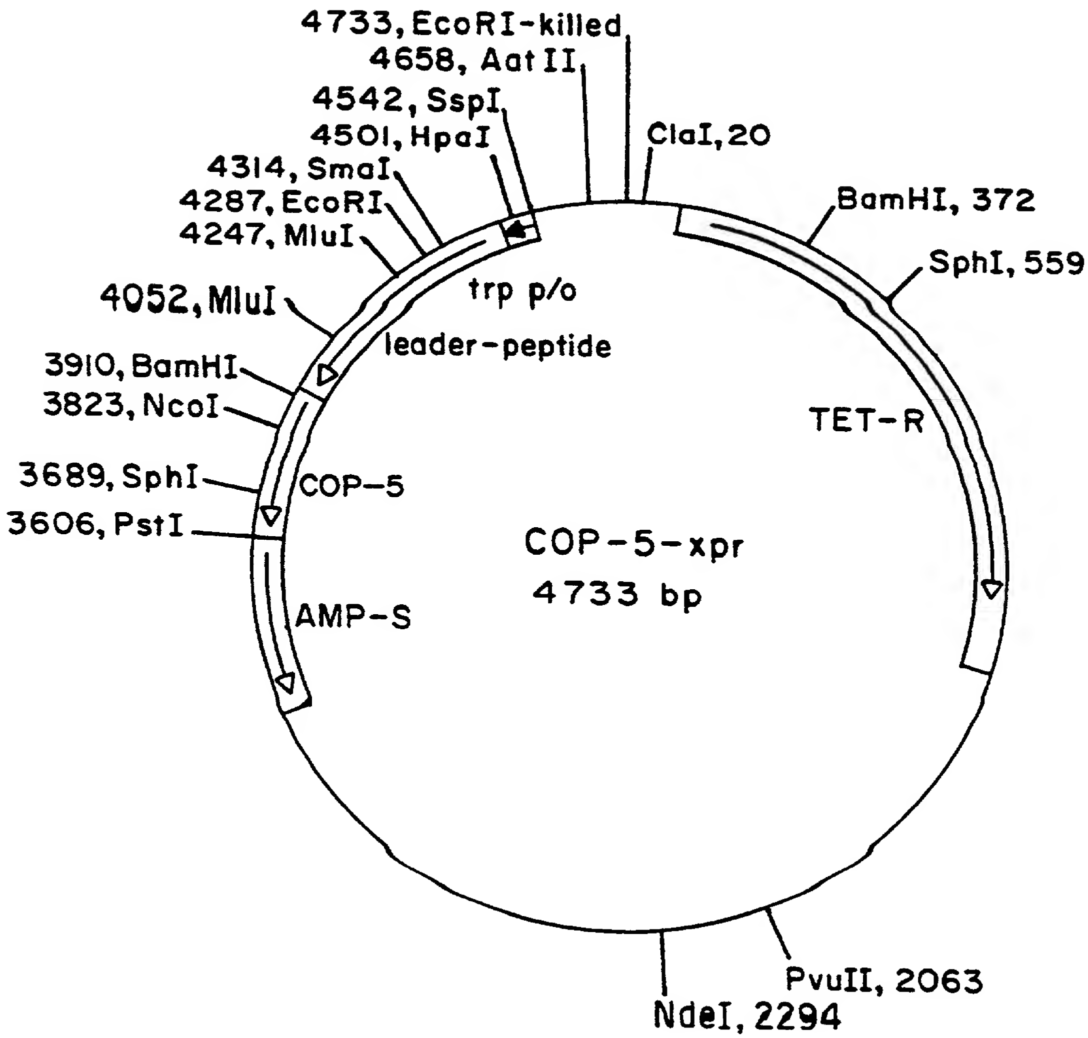
4733, EcoRI-killed
4658, AatII
4542, SspI
4501, HpaI
4314, SmaI
4287, EcoRI
4247, MluI
4052, MluI
3910, BamHI
3823, NcoI
3689, SphI
3606, PstI
ClaI, 20
BamHI, 372
SphI, 559
trp p/o
leader-peptide
TET-R
COP-5
AMP-S
COP-5-xpr
4733 bp
PvuII, 2063
NdeI, 2294

Fig. 21A

COP-5 fusion protein

```
             10         20         30         40         50
ATGAAAGCAATTTTCGTACTGAAAGGTTCACTGGACAGAGATCTGGACTC
 M  K  A  I  F  V  L  K  G  S  L  D  R  D  L  D  S
                                       BglII

             60         70         80         90        100
TCGTCTGGATCTGGACGTTCGTACCGACCACAAAGACCTGTCTGATCACC
  R  L  D  L  D  V  R  T  D  H  K  D  L  S  D  H

            110        120        130        140        150
TGGTTCTGGTCGACCTGGCTCGTAACGACCTGGCTCGTATCGTTACTCCC
L  V  L  V  D  L  A  R  N  D  L  A  R  I  V  T  P
      SalI                                      Sma

            160        170        180        190        200
GGGTCTCGTTACGTTGCGGATCTGGAATTCATGGCTGACAACAAATTCAA
 G  S  R  Y  V  A  D  L  E  F  M  A  D  N  K  F  N
I                         EcoRI

            210        220        230        240        250
CAAGGAACAGCAGAACGCGTTCTACGAGATCTTGCACCTGCCGAACCTGA
  K  E  Q  Q  N  A  F  Y  E  I  L  H  L  P  N  L
                 MluI         BglII    BspMI+

            260        270        280        290        300
ACGAAGAGCAGCGTAACGGCTTCATCCAAAGCTTGAAGGATGAGCCCTCT
N  E  E  Q  R  N  G  F  I  Q  S  L  K  D  E  P  S
                                HindIII

            310        320        330        340        350
CAGTCTGCGAATCTGCTAGCGGATGCCAAGAAACTGAACGATGCGCAGGC
 Q  S  A  N  L  L  A  D  A  K  K  L  N  D  A  Q  A
                 NheI                      FspI

            360        370        380        390        400
ACCGAAATCGGATCAGGGGCAATTCATGGCTGACAACAAATTCAACAAGG
  P  K  S  D  Q  G  Q  F  M  A  D  N  K  F  N  K

            410        420        430        440        450
AACAGCAGAACGCGTTCTACGAGATCTTGCACCTGCCGAACCTGAACGAA
E  Q  Q  N  A  F  Y  E  I  L  H  L  P  N  L  N  E
             MluI        BglII    BspMI+

            460        470        480        490        500
GAGCAGCGTAACGGCTTCATCCAAAGCTTGAAGGATGAGCCCTCTCAGTC
 E  Q  R  N  G  F  I  Q  S  L  K  D  E  P  S  Q  S
                      HindIII
```

Fig. 21B-1

```
        510       520       530       540       550
TGCGAATCTGCTAGCGGATGCCAAGAAACTGAACGATGCGCAGGCACCGA
 A  N  L  L  A  D  A  K  K  L  N  D  A  Q  A  P
      NheI                          FspI

        560       570       580       590       600
AGGATCCTAATGGGCTGTACGTCGACTTCAGCGACGTGGGCTGGGACGAC
K  D  P  N  G  L  Y  V  D  F  S  D  V  G  W  D  D
 BamHI               SalI

        610       620       630       640       650
TGGATTGTGGCCCCACCAGGCTACCAGGCCTTCTACTGCCATGGCGAATG
 W  I  V  A  P  P  G  Y  Q  A  F  Y  C  H  G  E  C
                         StuI         NcoI    BsmI+

        660       670       680       690       700
CCCTTTCCCGCTAGCGGATCACTTCAACAGCACCAACCACGCCGTGGTGC
 P  F  P  L  A  D  H  F  N  S  T  N  H  A  V  V
      NheI                          DraIII
                                   PflMI

        710       720       730       740       750
AGACCCTGGTGAACTCTGTCAACTCCAAGATCCCTAAGGCTTGCTGCGTG
Q  T  L  V  N  S  V  N  S  K  I  P  K  A  C  C  V
                                MSTII

        760       770       780       790       800
CCCACCGAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATGAGAA
 P  T  E  L  S  A  I  S  M  L  Y  L  D  E  N  E  K
                       SphI

        810       820       830       840       850
GGTGGTGCTGAAGAACTACCAGGAGATGGTAGTAGAGGGCTGCGGCTGCC
  V  V  L  K  N  Y  Q  E  M  V  V  E  G  C  G  C
                  PflMI

        860
GCTAACTGCAG
R  *
    PstI
```

Fig. 21B-2

Title: OSTEOGENIC DEVICES
Inventor(s): Oppermann et al.
Serial No. 09/754,831
Atty Docket No. STK-008CN
Atty/Agent: Patrick R.H. Waller/kkh
Express Mail Label No. EL902309562US

Fig. 22A

Fig. 22B